Toward Plug and Play Medical Cyber-Physical Systems

Insup Lee
PRECISE Center
School of Engineering and Applied Science
University of Pennsylvania

EMSIG Autumn School
Copenhagen, Denmark
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Penn Engineering

PRECISE
PENN RESEARCH IN EMBEDDED COMPUTING AND INTEGRATED SYSTEMS ENGINEERING

Trends in Medical Systems

Miniaturization

- Implantable devices
- Ingestible sensors

Interoperation

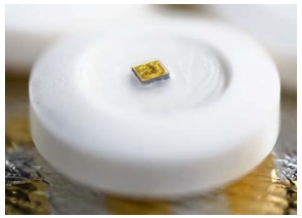
- Executable clinical scenarios
- Safety interlocks

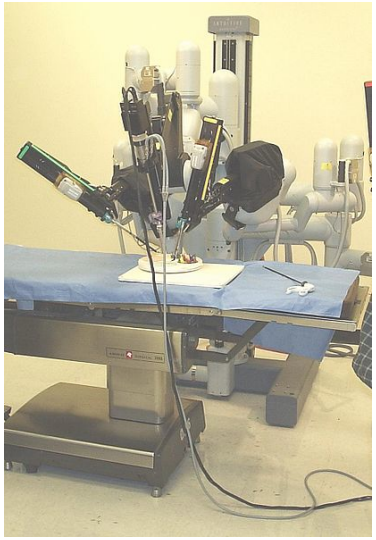
Teleoperation

- Tele-ICU
- Robotic surgery

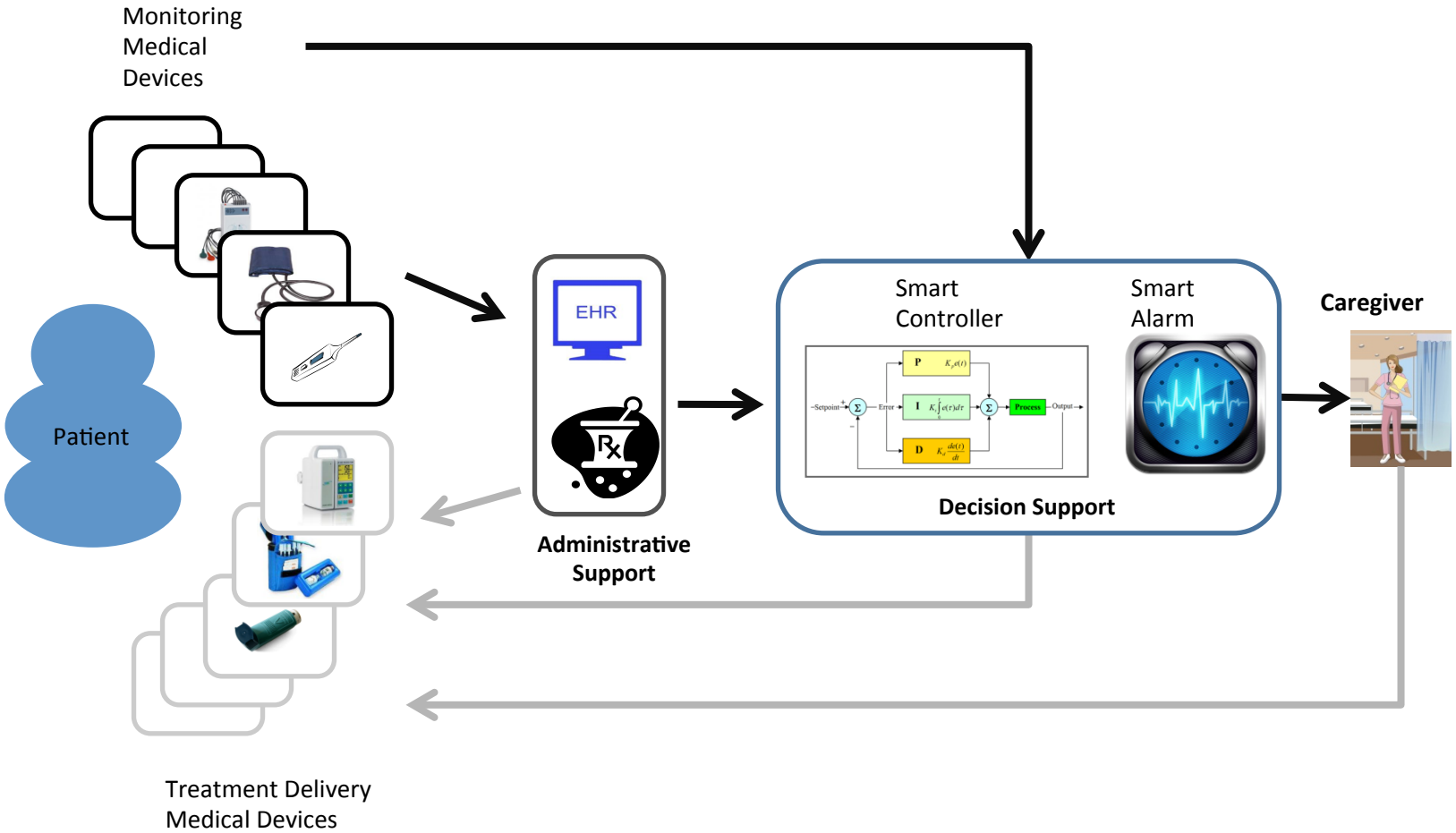
Autonomy

- Smart alarms
- Context-sensitive decision support
- Physiological closed loop control



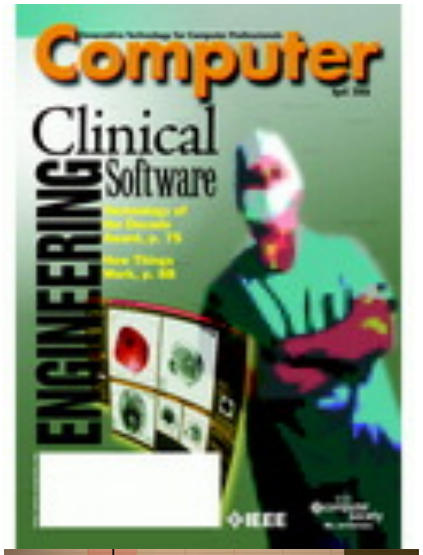


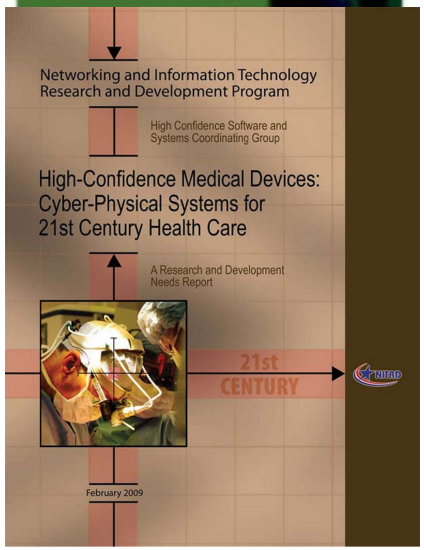
Overall Structure of MCPS



MCPS Research Challenges (partial list)

- Ensuring safety (and security)
  - Model-based and evidence-based development
  - Patient modeling and simulation
  - User-centered design
- Medical device integration and interoperation
- Adaptive patient-specific algorithms
- Incremental and compositional methods for certifiable assurance and safety



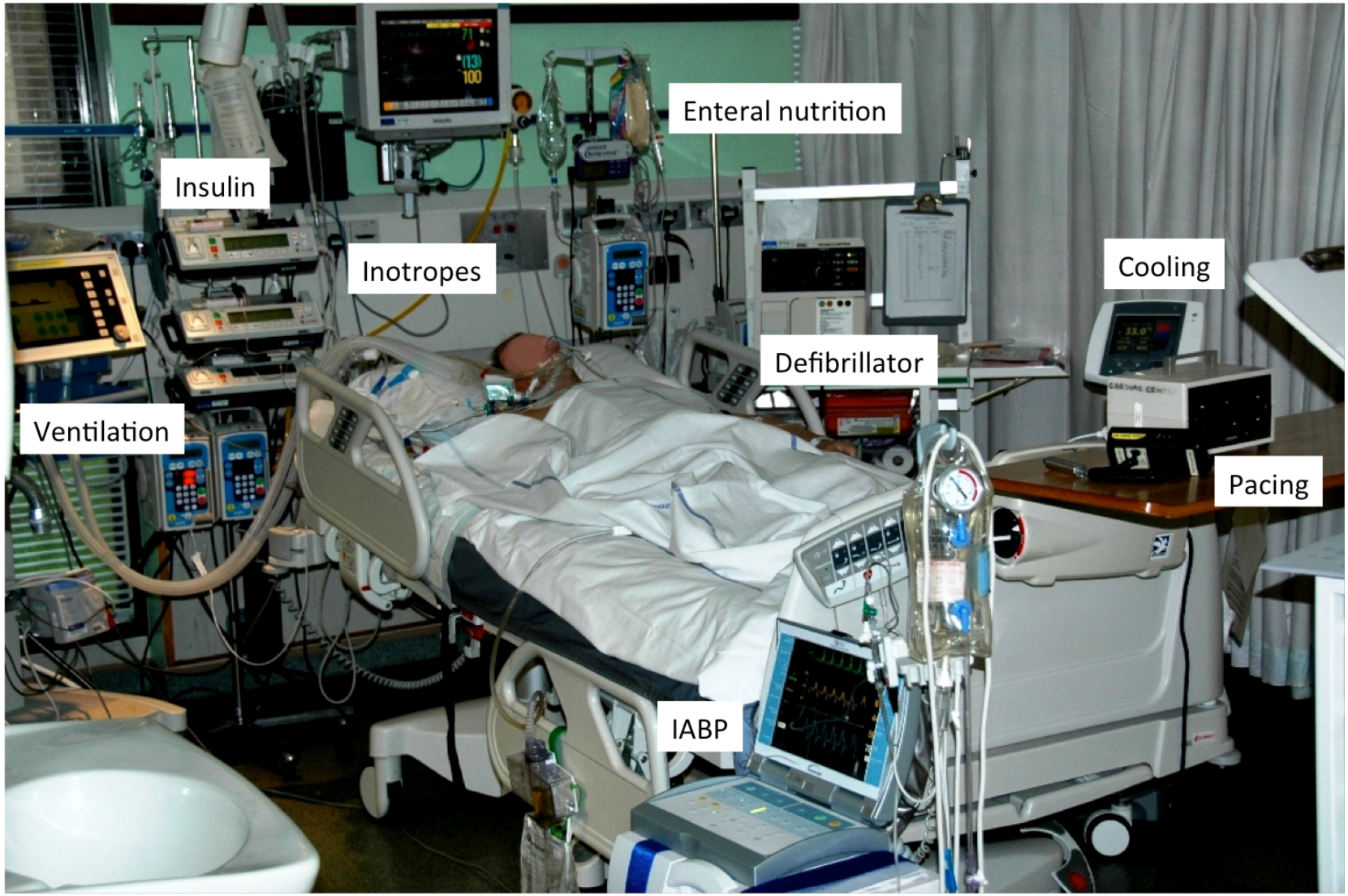


Outline

- Medical Device Interoperability
- PCA Case Studies
  - Generic PCA Infusion Pump
  - PCA Closed-Loop System
- Modeling and Analysis in Artificial Pancreas
  - Glucose Control Benchmark for Formal Verification
  - Data-driven Patient Behavior Modeling
- The Medical App Platform Approach for Safety Assurance

MEDICAL DEVICE INTEROPERABILITY

Example: ICU


Enteral nutrition
Insulin
Inotropes
Cooling
Defibrillator
Ventilation
Pacing
IABP

Current Problem

Little to no integration of Devices with each other:

- Humans must automate even simple clinical workflows
- Unnecessary burdens placed on human caregivers
- Few opportunities for "sensor fusion" (better alarms and diagnostics)

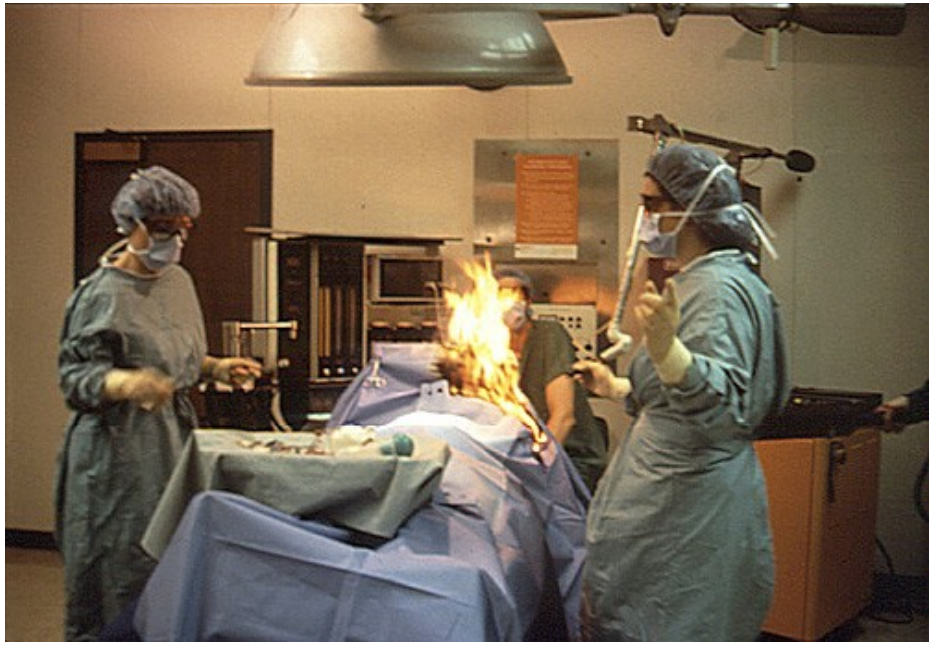
Clinical Scenario: Laser Surgery/Ventilator

Clinical Scenario: Medical Device Safetylock

Doctors enforce the following invariant:

- If laser = on then oxygen = off
- If patient's SpO2 < 95 then oxygen = on

Systems of Systems approach: let devices communicate and automate safety invariant enforcement



Clinical Scenario: X-Ray / Ventilator

"With the advent of sophisticated anesthesia machines incorporating comprehensive monitoring, it is easy to forget that serious anesthesia mishaps still can and do occur."
APSF Newsletter Winter 2005

Anesthesia Machine

Portable x-ray machine

Surgeons

What do laser-surgery/ventilator and X-ray/ventilator have in common?

They do not exist!

Why not?

Medical-Device Plug-and-Play

- A patient is treated using a variety of medical devices
  - Coordination between devices can increase safety or enhance functionality
  - Currently, caregivers coordinate devices

Current

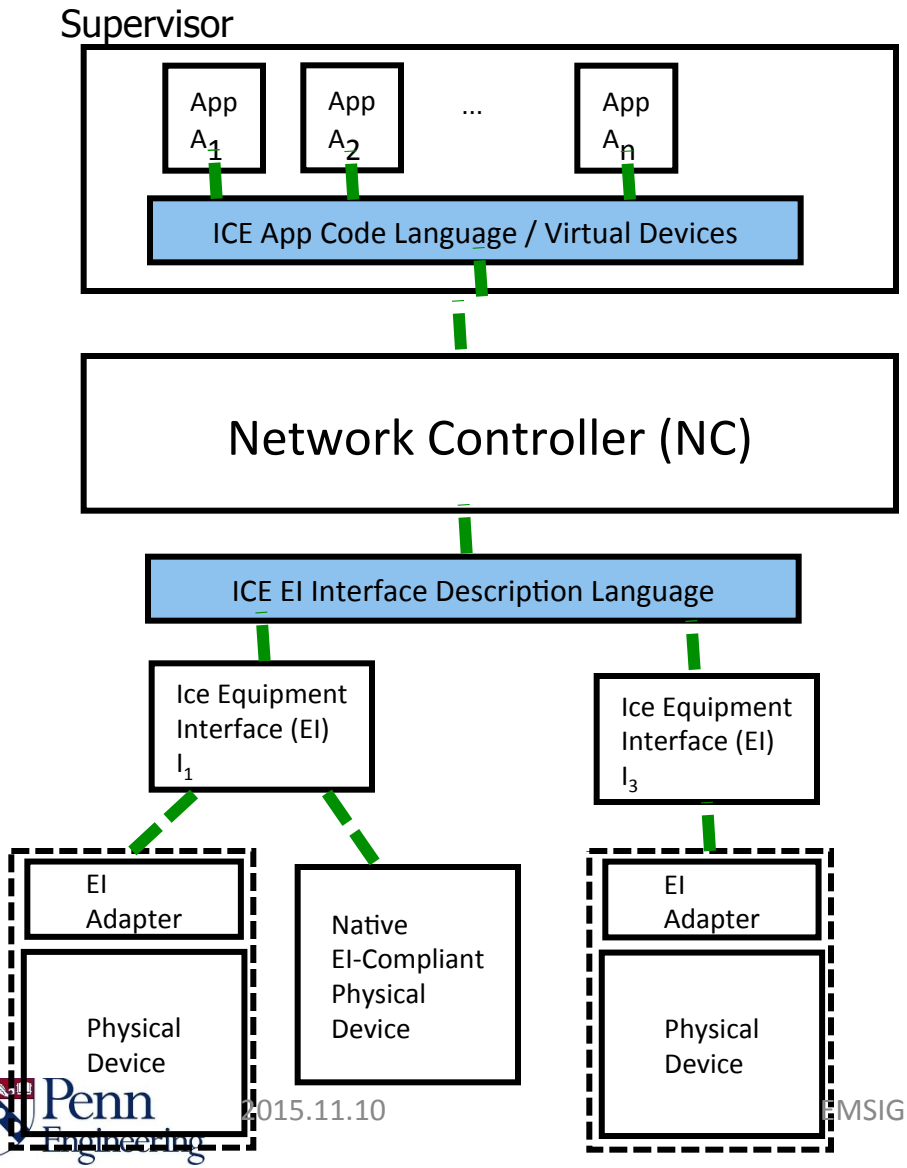
Future

- Interoperable devices can self-coordinate
  - Provide continuous monitoring
  - Handle routine tasks and respond to obvious problems
  - Alert caregivers in more serious cases
  - Physiological closed-loop control in many cases

- MD PnP
  - Interoperable medical devices based on plug-n-play
  - Vender neutrality based on open medical device interfaces
  - www.mdpnp.org

MEDICAL APPLICATION PLATFORM AND CLINICAL APPS

Integrated Clinical Environment (ICE)



- ASTM Standard F2761-2009 for ICE defines a high-level architecture and functional concept
- Subsequent standards are intended to provide specific functional and interfacing requirements for components
- The ICE architecture standard is the focal point for FDA's evaluation of MAP (Medical App Platfom) concepts in future medical systems
  - A key element of this evaluation is moving from regulation of "systems as a whole" to component-wise regulation

Virtual Medical Device (VMD)

- **MD PnP** enables the concept of **Virtual Medical Device:**
  - A set of medical devices coordinating over a network for clinical scenario.

Device Coordination Algorithm

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Medical Device Types

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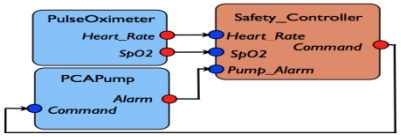
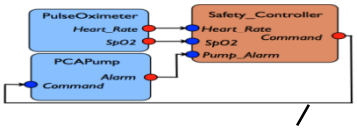
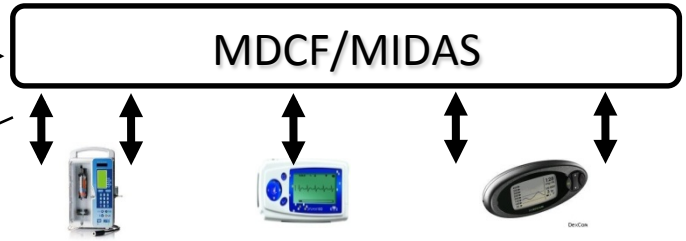
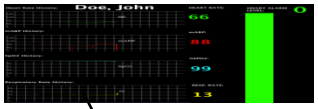


Virtual Medical Device (VMD)

- VMD does not physically exist until instantiated at a hospital.
- OpenICE and Medical Device Coordination Framework (MDCF)
  - prototype middleware for managing the correct composition of medical devices into VMD.



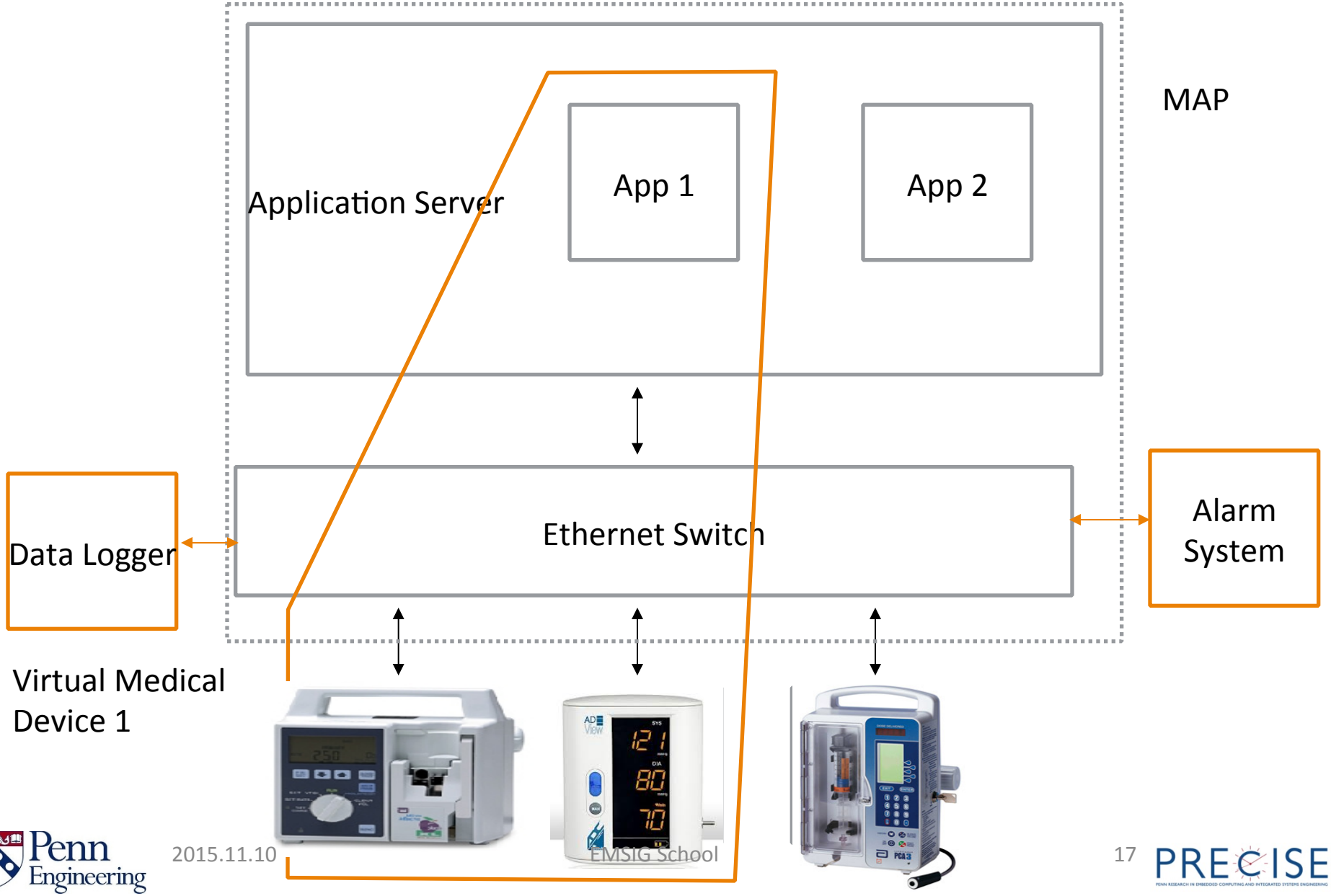




- Clinician selects appropriate VMD
- MDCF binds appropriate devices into VMD instance

MDCF displays VMD GUI for clinician

Architecture (Impl.)



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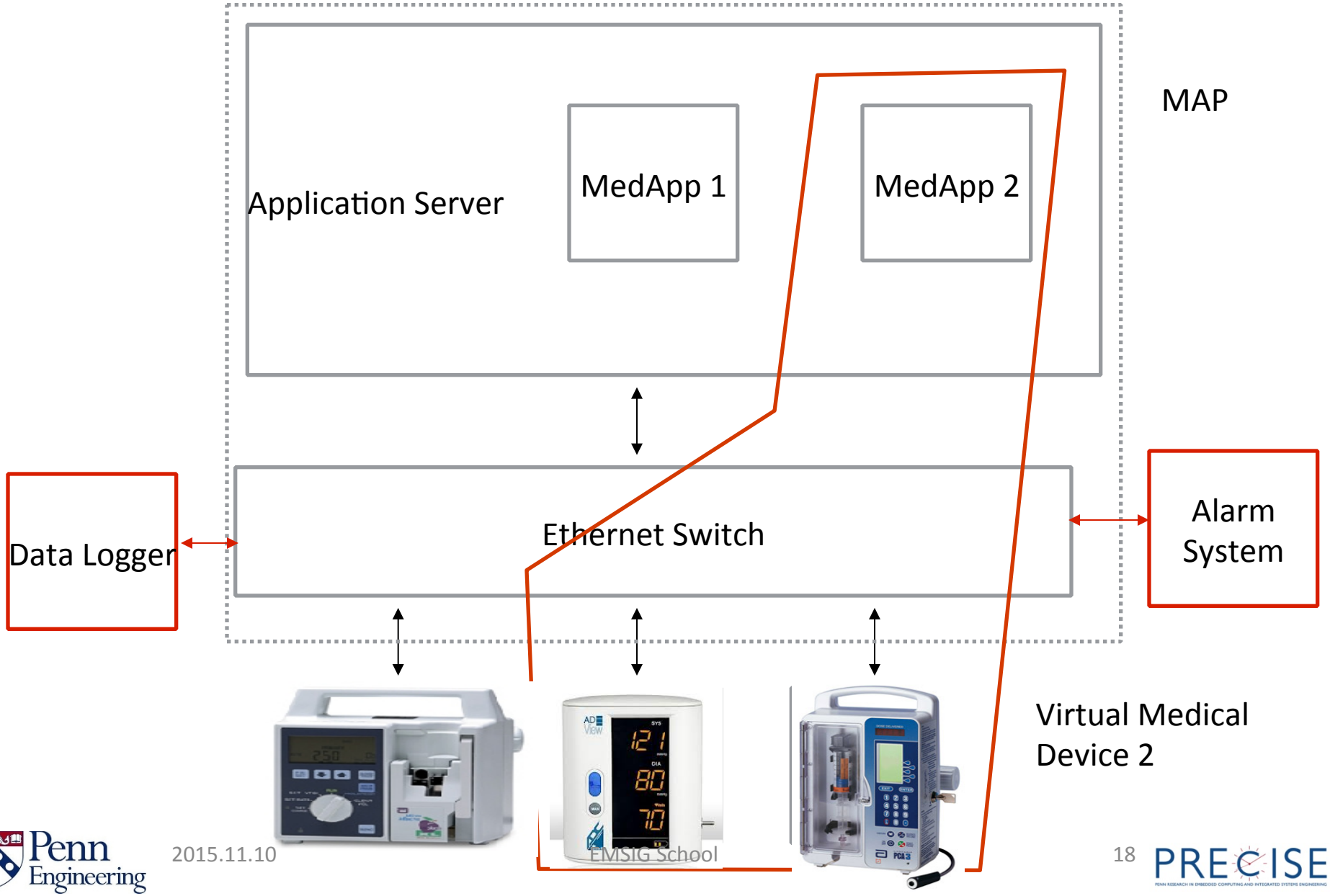


Example VMD apps

- Medical Device Coordination Apps
  - X-ray/Ventilator coordination
  - Laser/Ventilator coordination
- Smart Alarms
  - CABG (Coronary Artery Bypass Graft) Patients
- Physiological Closed-Loop Systems
  - PCA closed loop
  - BG closed loop

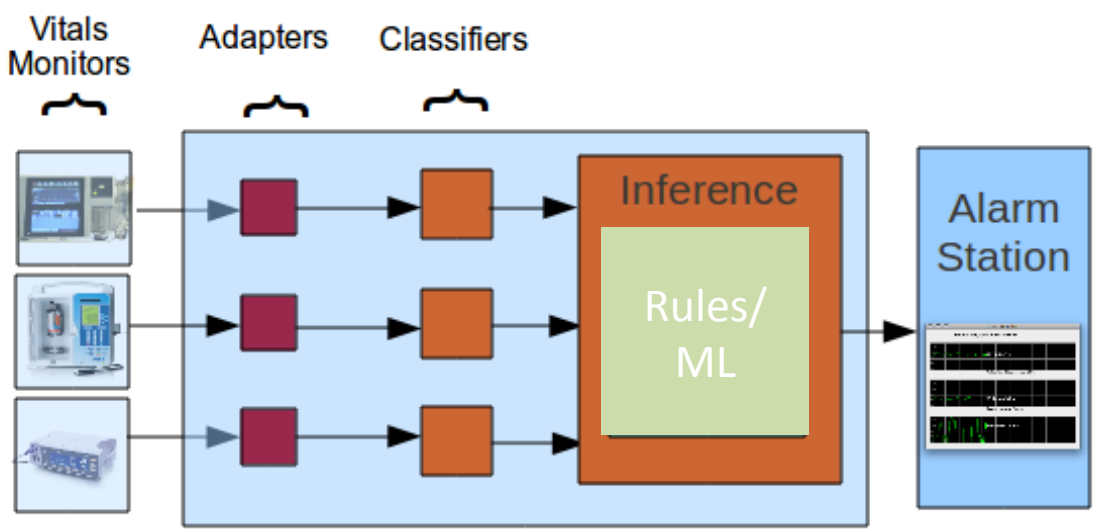
Case Study: ICU Smart Alarm

- Continuous monitoring of vital signs
  - creates deluge of data
  - mostly threshold alarms
- 57-99% of alarms are false
- Cause alarm fatigue
  - cause clinicians to ignore true alarms

False alarm rates: Kestin, et al: 75%, Phillips, et al: 86%, Clark et al: 99%,

Surgical ICU Smart Alarm

- Goal: Reduce Surgical ICU (SICU) False Alarms
  - Go beyond threshold alarms
- System structure
  - Capture 4 common vitals
    - HR, BP, RR, SPO_2
  - Use vitals together, instead of independently
  - Generate more useful alarms



SICU Smart Alarm Validation

- Initial Study (2010)
  - Create rules from clinicians
  - Test on retrospective data (Physionet)
  - 57% reduction in false alarms
- Secondary Study (2012)
  - IRB approved
  - Validate rules on data from UPHS patients
  - RA recorded alarm-prompted interventions
  - 45% reduction in false alarms

BP	HR	SPO_2	RR	Alarm Level
Normal	Normal	Normal	Normal	0
High	Normal	Normal	Low	1
High	Low	Normal	Normal	2
Very Low	Normal	Normal	High	3
High	High	Low	High	2

Table 1: Small subset of the rule set.

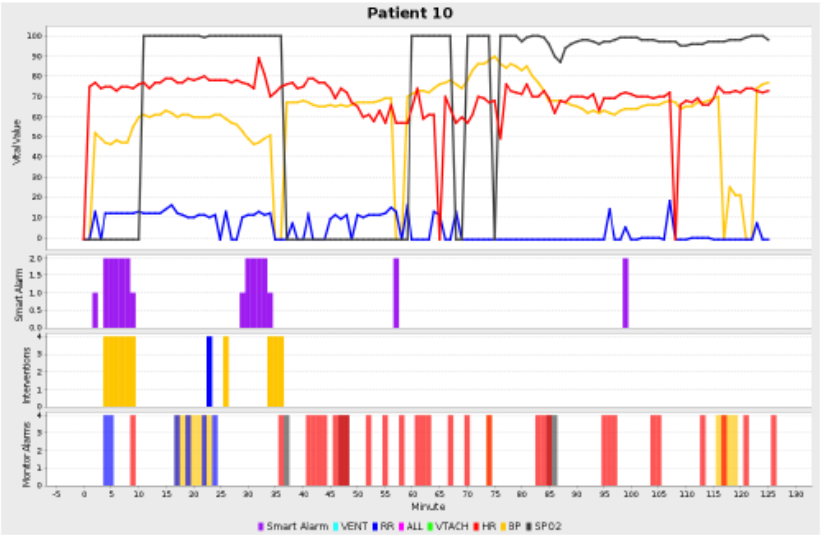
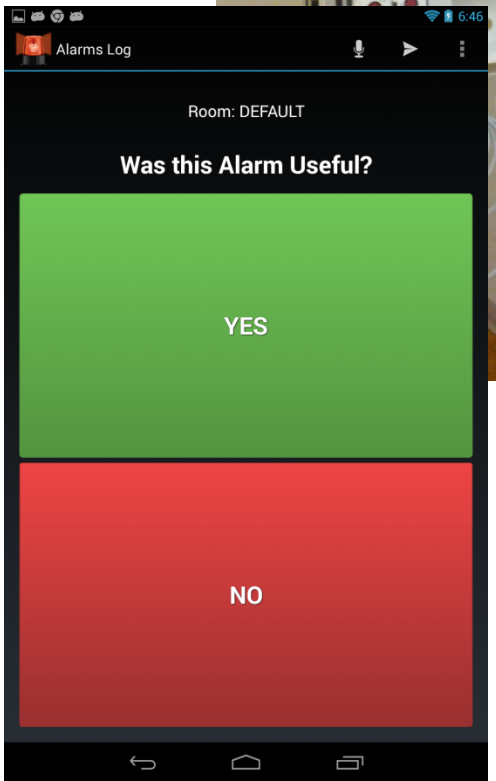


Fig. 3. Vitals signs and alarms; The top row is a trace of vital signs, smart alarm response is the second row, alarms resulting in an intervention are third from top and spurious alarms are in the bottom row. The smart alarm response tracks with the occurrence of intervention alarms.

SICU Smart Alarm Validation

- Current Study (Ongoing since 2014)
  - IRB Approved
    - ICU Bedside Monitors have Android tablets attached
    - 16 Bed SICU at Presbyterian SICU
  - Capture:
    - Vital signs
    - Generated alarms
    - Nurse annotations of alarm utility
    - Ground truth
  - Goal:
    - Further validate rule set
    - Use Machine Learning to create improved alarm algorithm



A L King, A Roederer, et al, "GSA: A framework for rapid prototyping of smart alarm systems, " in IHI 2010
A King, et al, "Evaluation of a Smart Alarm for Intensive Care using Clinical Data," in IEEE EMBS 2012

Smart Alarm Project

- Experiment goals
  - Determine which alarms are deemed useful by clinicians
    - Evaluate existing clinical **guidelines** as baseline
    - Evaluate current "smart alarm" based on **clinician expertise**
    - Use **machine learning** on dataset to further improve smart alarm

"Three-Pronged Approach"

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Clinical Guidelines

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Clinician Expertise

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Machine Learning

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PCA CASE STUDIES (SEE PART1)

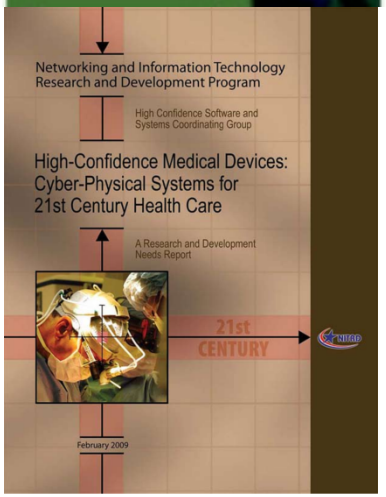
BG CONTROL SLIDES (SEE PART2)

SAFETY ASSURANCE FOR PLUG & PLAY MEDICAL SYSTEMS (SEE PART3)

MCPS Research at PRECISE Center

Goal: Develop a new development paradigm for the effective design and implementation of MCPS that are *safe*, *secure*, and *reliable*

- High-confidence medical software systems
  - Model-based development
  - GPCA (Generic Patient-Controlled Analgesia) infusion pump
  - Pacemaker
- Medical device interoperability
  - MDCF/MIDAS, VMD app (virtual medical device app)
  - Security and Privacy
- Smart alarms & clinical decision support
- Physiological closed-loop systems
  - Individualized care via patient modeling
  - Safety Analysis
- Assurance and Certification
  - Evidence-based certification
  - Blackbox recorder for medical device



Selected References

- Platform-Specific Code Generation from Platform-Independent Timed Models, BaekGyu Kim, Lu Feng, Oleg Sokolsky and Insup Lee, IEEE RTSS, Dec 2015. (to appear)
- A Data-Driven Behavior Modeling and Analysis Framework for Diabetic Patients. Sanjian Chen, Lu Feng, Michael Rickels, Amy Peleckis, Oleg Sokolsky and Insup Lee. IEEE Int. Conf. on Healthcare Informatics (ICHI), Oct. 2015.
- An Intraoperative Glucose Control Benchmark for Formal Verification. Sanjian Chen, Matthew O'Kelly, James Weimer, Oleg Sokolsky, Insup Lee. ADHS (IFAC Conf. on Analysis and Design of Hybrid Systems), Oct 14-16, 2015.
- Towards Assurance for Plug & Play Medical Systems, Andrew L. King, Lu Feng, Sam Procter, Sanjian Chen, Oleg Sokolsky, John Hatcliff, Insup Lee, SAFECOMP, Sept 2015.
- A Safety Argument Strategy for PCA Closed-Loop Systems: A Preliminary Proposal, Lu Feng, et al., MedCPS Workshop, April 14, 2014.
- Distributed aspects of the artificial pancreas, S.D. Patek, S. Chen, P. Keith-Hynes, I. Lee, *51st Annual Allerton Conference on Communication, Control, and Computing*, Oct 2013.
- Model-Driven Safety Analysis of Closed-loop Medical Systems, Miroslav Pajic, et al., In *IEEE Transactions on Industrial Informatics*, 2013.
- A Model-Based I/O Interface Synthesis Framework for the Cross-Platform Software Modeling, BaekGyu Kim, et al., *IEEE RSP,* October 2012.
- Evaluation of a Smart Alarm for Intensive Care using Clinical Data. Andrew King, et al. In *34th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC'12)*, September, 2012.
- A Safety Case Pattern for Model-Based Development Approach, Anaheed Ayoub, Baek-Gyu Kim, Insup Lee and Oleg Sokolsky. *NASA Formal Methods Symposium (NFM)*, April 2012.
- Challenges and Research Directions in Medical Cyber-Physical Systems, Insup Lee, et al. In *Special Issue on Cyber-Physical Systems, Proceedings of the IEEE*, Volume 100, Issue 1, pp.75-90, January 2012.
- Safety-Assured Development of the GPCA Infusion Pump Software, BaekGyu Kim, et al., *EMSOFT 2011*, October 2011.

- Additional related papers at www.cis.upenn.edu/~lee/home/publications/

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Thank You!
Questions?

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